16. (Amended) The nucleic acid molecule of claim **[1] 4**, wherein the modulator module has a portion comprising one of the mistletoe lectin B chain, a fragment thereof, a derivative thereof, the peptide KDEL **(SEQ ID NO:35)**, and the peptide HDEL **(SEQ ID NO:36)**.

26. (Amended) The host of claim 25, wherein the eukaryote is selected from the group consisting of a *Saccharomyces* **[sp.] species**, an *Aspergillus* **[sp.] species**, a *Spodoptera* **[sp.] species**, and *Pichia pastoris*.

REMARKS

Claims 1-27, 29, and 32-37 are pending in the present application. Claims 28, 30, 31, and 38-46 have been withdrawn by the Examiner as being drawn to a non-elected invention. Claims 8, 15, 16, and 26 have been amended. These amendments do not include new matter as detailed below. For the Examiner's convenience, a list of the pending, non-withdrawn claims, as amended to date, is included with this Amendment.

Support in the Specification

The specification has been amended at page 22, line 29, to add an apostrophe which was inadvertently omitted. Support for this amendment is found in originally-filed claim 8, in which the apostrophe appears, and in the accompany abstract from Fersht, (1985, Enzyme Structure and Mechanism, 2d ed., W.H. Freeman and Co., New York, at pp. 29-30), which demonstrates that the skilled artisan would understand the standard notation used to denote amino acid residues in proteolytic cleavage sites. The skilled artisan would therefore realize that it was the omission of the apostrophe on page 22 of the specification that was inadvertent, rather than inclusion of the apostrophe in originally-filed claim 8.

Claims 8 and 16 have been amended to add the SEQ ID NO: designations for the sequences recited in the claims.

Claim 8 was also amended to recite that S1' can be any amino acid residue. This recitation is supported in the specification at page 22, line 28, through page 23, line 9, where the identity of every residue of the recited sequence except S1' is set forth. From the context of the application (the recited sequence being a proteolytic cleavage site), the indication of the cleaved bond (i.e., "/"), and what was known in the art (see Fersht, 1985, Enzyme Structure and Mechanism, 2d ed., W.H. Freeman and Co., New York, at pg. 30, section d; copy enclosed), the skilled artisan would understand that the identity of residue S1' is irrelevant. Thus, the skilled artisan would understand that S1' can be any amino acid residue, as explicitly recited in the amended claim.

Claims 15 and 16 have been amended to depend from claims 7 and 4, respectively. Claim 15 has also been amended to indicate trademarks. Claim 26 has been amended to delete the abbreviation "sp." and spell out the term "species". The Applicants contend that these amendments are non-substantive and do not require explicit support in the specification.

Objections

In item 2 of the Office Action, the Examiner objects to the title of the invention. According to the Examiner, the title is not descriptive. The Applicants have amended the title to indicate that the claims are directed to nucleic acids.

In item 3 of the Office Action , the Examiner objects to claims 8 and 16 for failing to indicate SEQ ID NO: designations. Claims 8 and 16 have been amended to include SEQ ID NO: designations.

The Applicants respectfully submit that these amendments overcome the Examiner's objections, and request reconsideration and withdrawal of these objections.

Rejection of claims 32 and 33 pursuant to 35 U.S.C. § 101

In items 4 and 5 of the Office Action, the Examiner rejects claims 32 and 33 pursuant to 35 U.S.C. § 101. In the Examiner's view, the specification fails to disclose a credible or well-established utility. The Applicants respectfully contend that the Examiner is not properly

applying the Office's Interim Written Description Guidelines (IWDG), promulgated in December 1999. According to the IWDG, the Examiner should find the invention recited in each of claims 32 and 33 to have patentable utility if the subject matter has a "well established" utility or a utility "asserted" in the specification, and if the asserted or established utility is "specific, substantial, and credible." Each of these issues is discussed in greater detail in the Offices "Revised Interim Utility Guidelines Training Materials" (RIUGTM; prepared by the Office for use by Examiners and available at http://www.uspto.gov/web/menu/utility.pdf). The Applicants discuss each element required for a finding of utility in the ensuing paragraphs.

"Well Established" Utility

The RIUGTM indicates that a "well established" utility is one which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. Each of the medicament of claim 32 and the kit of claim 33 comprises a nucleic acid molecule as recited in claim 1. Claim 1 recites that that nucleic acid molecule encodes a fusion protein which comprises an effector module that is intracellularly cytotoxic. The Applicants contend that it would be immediately apparent to the skilled artisan that the nucleic acid molecule recited in claim 1 is useful for killing non-desired cells (i.e. by delivering the nucleic acid molecule to the interior of the cell and expressing the encoded fusion protein therein). Thus, the Applicants contend that the uses for the medicament and kit of claims 32 and 33 would be immediately apparent to the skilled artisan.

"Asserted" Utility

The Applicants direct the Examiner's attention to the specification at page 10, lines 10-15, and at page 12, lines 18-22, where uses for the medicaments and kit comprising a nucleic acid recited in claim 1 are explicitly disclosed. The Applicants therefore contend that uses for the medicament and kit of claims 32 and 33 have been asserted in the specification.

"Specific" Utility

The RIUGTM indicates that a "specific" utility is one which is 'specific' to the claimed subject matter, in that it is not a utility applicable to a broad class of subject matter having no relationship to the invention. The specification discloses (e.g., at page 12, lines 17-25) that the physiological effect associated with the nucleic acid molecule is attributable to the mistletoe lectin A activity of the encoded fusion protein, which can induce apoptosis in cells. The Applicants therefore contend that the utility of the medicament and kit of claims 32 and 33 is "specific" to the claimed subject matter.

"Substantial" Utility

The RIUGTM indicates that a "specific" utility is a "real world" use. The RIUGTM specifically identifies a therapeutic method of treating a disease as a substantial utility. The Applicants believe that it follows the compositions (including medicaments and kits) for treating a disease also have substantial utility. As set forth above with regard to "well established" utility, the Applicants contend that therapeutic uses for the medicament and kit recited in claims 32 and 33 would be immediately obvious to the skilled artisan. Furthermore, the Applicants contend that therapeutic uses have been explicitly asserted in the specification, as set forth above with regard to "asserted utility." The Applicants therefore contend that the medicament and kit recited in claims 32 and 33 have a "substantial" utility.

"Credible" Utility

The RIUGTM indicate that a utility is "credible" if it is believable to a person of ordinary skill in the art based on the totality of evidence and reasoning provided. The Examiner has not asserted any reason why the skilled artisan (or even the ordinarily skilled artisan, as the RIUGTM inaccurately states the test) would doubt that the nucleic acid molecule recited in claim 1 (or medicaments and kits which comprise that molecule) could be used for their asserted or immediately apparent purposes. With regard to the Examiner's comments regarding difficulties known in the art for gene therapy methods, the Applicants note that the Examiner's concerns do not relate to whether the claimed nucleic acid molecules, medicaments, and kits can be used for

their asserted and apparent purposes, but rather involve how well or easily they could be used for those purposes. The Applicants therefore contend that, in the absence of an assertion by the Examiner of a reason why the skilled artisan would doubt the operability of the medicament and kit of claims 32 and 33 for their asserted and apparent uses, the Examiner's utility rejection cannot be sustained.

For the reasons set forth in the sub-sections above, the medicament and kit of claims 32 and 33 have specific, substantial, and credible utility that is both immediately apparent to the skilled artisan (and therefore "well established) and asserted by the Applicants in the specification. Thus, claims 32 and 33 comply with the utility requirement of 35 U.S.C. § 101. Reconsideration and withdrawal of the Examiner's rejection are respectfully requested.

Rejection of Claims 32 and 33 Pursuant to 35 U.S.C. § 112, First Paragraph

Claims 32 and 33 stand rejected pursuant to 35 U.S.C. § 112, first paragraph. In the Examiner's view, these claims are not enabled both i) because the claims fail to satisfy § 101 (i.e., the specification cannot have taught how to use the claimed subject matter, which the Examiner asserts has no utility) and ii) because the skilled artisan could not practice the claimed invention without undue experimentation.

The Applicants believe that the response to the rejection of claims 32 and 33 pursuant to 35 U.S.C. § 101 set forth in the previous section should alleviate the Examiner's concern regarding the first ground (lack of utility) for the Examiner's rejection pursuant to 35 U.S.C. § 112, first paragraph. For this reason, the Applicants concentrate the following remarks on the Examiner's assertion that undue experimentation would be necessary to practice the invention in claims 32 and 33. Since the Examiner has discussed enablement in terms of individual *Wands* factors, the Applicants have mirrored this format in the following sub-sections.

Claims 32 and 33 recite a medicament and a kit, respectively, comprising a nucleic acid recited in claim 1. The Examiner does not appear to have asserted that the skilled artisan would be unable to make the recited medicaments and kits. The Applicants believe that it is immediately apparent to the skilled artisan how the medicaments and kits can be made in view

of the disclosure in the specification. For this reason, the Applicants assume that the Examiner's enablement rejection reflects a belief by the Examiner that the specification fails to teach the skilled artisan how to use the medicaments and kits. Briefly stated, the Applicants' response is that the Examiner inappropriate considers uses of medicaments and kits to be similar and that the Examiner concentrates too intently on methods of treatment (which are not recited in either claim 32 or 33).

Nature of the Invention

The Examiner recognizes that the medicament can be used in methods of treating a patient. The Examiner's understanding of the medicament recited in claim 32 seems to be at least basically correct, although the protein encoded by the vector need not be both processed and cleaved in the cell to which the vector is delivered. Processing of the encoded protein comprises cleavage of the processing module (i.e., processing can mean cleavage alone).

With regard to the kit recited in claim 33, the Applicants respectfully contend that the kit has uses other than methods of treating a patient. For example, the specification discloses that host cells (preferably prokaryotic host cells) can be used to propagate vectors disclosed in the specification or to express proteins encoded by such vectors (i.e., so that the proteins can be used in various ways; see page 27, lines 11-24). The Applicants respectfully contend that expression in prokaryotic cells of a protein encoded by a vector is a routine procedure, and that the 'nature of the invention' with regard to the kit is that kits of the general type recited in claim 33 are common and predictably useful.

Breadth of the Claims

The Applicants respectfully contend that the Examiner misconstrues the scope of claims 32 and 33. Claim 32 recites a medicament comprising two vectors. Claim 33 recites a kit comprising two vectors. Neither of claims 32 and 33 recites a method of treatment. Although the composition of the recited vectors can vary, as disclosed in the specification, the methods of using the recited medicaments and kits does not substantially vary regardless of the particular composition. Insofar as claims 32 and 33 are concerned, it does not matter if the medicaments

and kits are used in conjunction with a single disease state or a variety of disease states - the methods of making and using those medicaments and kits are the same. The Examiner is requested to recognize that the enablement requirement is satisfied by describing how to make and use the medicament recited in claim 32 and the kit recited in claim 33. The Applicants are not required to disclose every possible disease state (or other physiological state) for which the medicaments and kits might be used; the methods of making and using those medicaments and kits are disclosed.

State of the Prior Art

The Examiner cites purportedly prior art beliefs that gene therapy protocols had not been 'routinely' successful in treatment of human diseases. The Applicants respectfully contend that the Examiner's observation is misplaced in several regards. First, the Examiner will recognize that a patent application need not teach how to make and use the claimed invention to the degree that its manufacture and use would be considered 'routine.' All that the Applicants are required to do is to teach the skilled artisan to make and use the invention. Second, the Examiner appears to implicitly admit that gene therapy methods are not abject failures, but rather that the efficacy of prior art gene therapy protocols leaves room for improvement. Put another way, the Applicants understand the Examiner to allege that gene therapy protocols do not work well, not that they do not work at all. There is, of course, no requirement in the first paragraph of 35 U.S.C. § 112 (or elsewhere in the statute) that an applicant must teach how to make and use the claimed invention such that it works well. The Applicants need only teach the skilled artisan how to make and use the claimed invention.

Regardless of whether the medicament recited in claim 32 works well, poorly, or at an intermediate level of efficacy, the skilled artisan would have no reason to doubt that the Applicants have taught how to make and use it. Because the Applicants have not recited any particular level of efficacy in claim 32, the Examiner has no grounds upon which to require any particular level of efficacy greater than mere operability. The Applicants respectfully contend that the Examiner has not provided any reasonable basis to assert that the Applicants have not

taught how to use the medicament recited in claim 32, and that rejection of this claim in view of the enablement requirement is inappropriate.

As noted above, the kit recited in claim 33 has a variety of uses, including propagation of the vector described in the application and expression of the protein encoded by that vector. The Applicants do not understand the Examiner to assert that these methods are not within the ken of the skilled artisan, given the description provided for the vector in the specification. Thus, the Applicants do not believe that a skilled artisan would have any difficulty making and using the kit recited in claim 33, and that rejection of this claim in view of the enablement requirement is also inappropriate.

Working Examples and Guidance in the Specification

The Examiner observes that no working examples of methods of treating a human are disclosed in the specification. The Applicants respectfully contend that the Examiner's observation is not relevant to the patentability of what is claimed. Claim 32 recites a medicament. Claim 33 recites a kit.

As noted above, the vectors recited in the kit of claim 33 can be used to propagate the vector or to express the protein encoded thereby in a producer cell. Examples 1 through 4 (pages 40-45 of the specification) demonstrate the operability of the vector (and, implicitly, a kit comprising it) for these purposes. Examples 5 and 6 demonstrate the operability of proteins expressed using the vector. Thus, the Applicants respectfully contend that Examples 1 through 6 demonstrate that the Applicants have disclosed how to make and use the kit recited in claim 33.

With regard to the medicament recited in claim 32, the Applicants first note that ethical considerations require testing of medicaments in non-human systems prior to testing in humans. The Applicants further note that there is no requirement in U.S. patent law that a compound or composition that is claimed in a patent application to exhibit therapeutic properties be tested in humans prior to allowance of the claims or filing of a patent application directed to the compound or composition. The Applicants need only teach how to make the medicament recited in claim 32 and how to use it. The Examiner does not appear to suggest that the Applicants have not taught how to make the medicament. The Applicants respectfully contend

that the specification discloses how the medicament is to be used (see page 27, lines 5-10, and page 30, lines 1-15), namely, by delivery of a vector to a target cell and expression of the encoded protein therein. The Applicants need teach no more. The skilled artisan would understand that expression of the protein in the cell can alleviate any of the conditions disclosed in the specification (for example at page 10, lines 10-15).

Predictability of the Art

The Examiner acknowledges that physiological systems are, in an abstract sense, unpredictable. However, the Applicants are not claiming a vague physiological system. Instead, the medicament and kit of claims 32 and 33 recite a nucleic acid having defined portions having predictable properties. The Examiner has not asserted that the protein regions defined by the recited portions (i.e., modules) of the nucleic acids would exhibit properties other than those attributed to them by the Applicants. Thus, the Applicants believe that the Examiner does not contest the predictability of the activity of the encoded proteins. Instead, the Examiner appears to question the predictability of vector delivery to cells and expression of the vector therein.

The Applicants respond that the skilled artisan would not believe the claimed vectors to be inoperable for purposes of delivery to cells and expression therein. Thus, the Examiner's concerns appear to be directed to the degree of efficacy, rather than to whether the vectors would be operable. As noted above, this analysis misses the point of the enablement requirement. The Applicants need only teach the skilled artisan how to make and use the claimed invention, not how to make and use the claimed invention well in every conceivable circumstance. The Applicants believe that they have satisfied this burden with respect to the medicament and kit recited in claims 32 and 33.

Amount of Experimentation Necessary

The Applicants' comments with regard to the Examiner's comments in the section of the office action (i.e., last paragraph on page 4) corresponding to the amount of experimentation necessary to practice the invention substantially mirror those made above. Briefly, the Examiner appears to be focusing on whether the claimed invention will work well

(e.g., well enough to be approved by U.S. regulatory agencies for treatment of humans), rather than, more properly, on whether the Applicants have taught the skilled artisan how to make and use the claimed medicament and kit. Crudely summarized, the Applicants have taught that delivery of a protein or nucleic acid disclosed in the present application to a cell can have desirable properties (e.g., apoptosis of a diseased or disease-causing cell). The Applicants have also taught (directly and by reference to the work of others) methods of providing those proteins and nucleic acids to cells. There is no requirement that the Applicants undertake "extensive research to understand the fundamental biology of the system" (which system?) or that they "ultimately develop therapeutic methods," as suggested by the Examiner.

The Applicants need only teach how to make and use what they have claimed. The Applicants respectfully contend that they have taught how to make and use the medicament and kit recited in claims 32 and 33, and that the Examiner has provided no objective reason why one skilled in the art would believe that they have not. Should the Examiner be privy to information that would demonstrate the inoperability of the medicaments and kits recited in claims 32 and 33, then the Examiner is required to either cite the public source of that information or put the Examiner's non-public knowledge into the form of an affidavit in which that information is expressly set forth. If, on the other hand, the Examiner's concern is limited to the observation that future developments by the inventors or others may render the medicament and kit of claims 32 and 33 even more reliably efficacious than those explicitly disclosed in the specification, then the Examiner must recognize that he is applying a standard greater than that set forth in the first paragraph of 35 U.S.C. § 112. The Applicants believe that the Examiner questions the degree to which the efficacy of the claimed medicament and kit have been optimized, rather than their operability. Reconsideration and withdrawal of the Examiner's rejection of claims 32 and 33 pursuant to 35 U.S.C. § 112, first paragraph, are respectfully requested for these reasons.

Rejection of Claims 1-27, 29, and 34-37 Pursuant to 35 U.S.C. § 112, First Paragraph

Claims 1-27, 29, and 34-37 stand rejected by the Examiner pursuant to 35 U.S.C. § 112, first paragraph. In the Examiner's view, the subject matter of these claims is not enabled

by the specification. The Examiner asserts that the specification does not adequately enable nucleic acids encoding fusion protein "fragments" and "derivatives" and fusion proteins which exhibit "deletions," "substitutions," "insertions," "additions," and "exchanges." The Applicants respectfully disagree.

The Examiner observes that these fusion proteins include all homologs, fragments, and synthetic variants of the recited amino acid sequence, and that the specification does not explicitly list the sequence of every fusion protein encompassed by the claims. However, the Examiner incorrectly asserts that the specification fails to reveal the specific properties of functional effector, processing, modulating, targeting, and affinity modules. The Applicants respectfully assert that the specification sets forth the required properties of each of these modules (e.g., in the paragraph bridging pages 11 and 12 for the 'effector' module) and methods of determining, with no more than routine experimentation, whether any particular homologue, fragment, or synthetic variant exhibits those properties (e.g., in Examples 1-13).

The Examiner observes that "predicting which fragments or derivatives of a protein will retain functionality and which will not is complex and well outside the realm of routine experimentation." Regardless of whether this is true, there is no need to 'predict' whether any particular fragment or derivative will exhibit the properties required for the corresponding module, since the Applicants have disclosed how a skilled artisan can test the fragment or derivative in order to determine the presence or absence of those properties. The Applicants respectfully contend that they are required to do no more.

With regard to the Examiner's comments regarding the enablement of claims 25 and 26, the Applicants are unable to find the portion of the specification to which the Examiner refers for the proposition that the non-glycosylated proteins are preferred. The Applicants note that the specification discloses one or more advantages of non-glycosylated fusion proteins (e.g., reduced hepatotoxicity, as disclosed at page 15, lines 9-13). However, the specification clearly discloses (e.g., at page 27, lines 19-24) that the fusion protein can be produced in eukaryotic cells. Even if the Examiner's assertion that non-glycosylated fusion proteins can be more efficiently cleaved intracellularly is accurate, the Applicants respectfully contend that this observation is irrelevant to enablement of claims 25 and 26. The Applicants are entitled to claim

both 'more efficient' and 'less efficient' embodiments of their invention. The Examiner has not asserted that the host cells of claims 25 and 26 would be inoperative if the fusion protein were glycosylated, only (apparently) that they would be less preferable than other host cells. This is not non-enablement. The Applicants respectfully contend that the glycosylation state of fusion proteins in the host cells recited in claims 25 and 26 is irrelevant to whether those claims are enabled by the specification.

For the foregoing reasons, the Applicants respectfully request that the Examiner reconsider and withdraw the rejection of claims 1-27, 29, and 34-37 pursuant to 35 U.S.C. § 112, first paragraph, for lack of enablement.

Rejection of claims 1-27, 29, and 34-37 pursuant to 35 U.S.C. § 112, first paragraph

Claims 1-27, 29, and 34-37 also stand rejected by the Examiner for failure to meet the written description requirement of 35 U.S.C. § 112, first paragraph. The Examiner correctly recognizes that one of the purposes of the written description requirement is to ensure that an inventor was "in possession" of the claimed invention as of the time the application was filed. However, the Applicants respectfully contend that the Examiner misinterprets "possession." The Examiner appears to believe the Applicants were "in possession" of only the subject matter in short list (items A-E) on page 7 of the office action. Thus, the Examiner appears to interpret 'possession' as 'physical possession.' The Applicants respectfully contend that this interpretation is erroneous.

The Applicants respectfully contend that 'possession' of an invention is satisfied by conception of the invention. No actual reduction to practice (i.e., physical possession) of an invention is necessary for the act of invention to have occurred according to U.S. patent law. Thus, the Examiner's apparent interpretation of 'possession' cannot be correct. The Applicants respectfully contend that their conception of the invention, throughout its scope, occurred no later than the filing date of the present application. The subject matter included within the scope of the claims (i.e., including "fragments," "derivatives," etc., of the explicitly disclosed fusion proteins and nucleic acids encoding them) includes, as discussed in a previous section of this Amendment, nucleic acids encoding a fusion protein having the recited modules. The structure

of each of those modules is based on disclosed polypeptide sequences, and the properties which every fragment (derivative, etc.) must exhibit in order to be within the scope of the claim is disclosed. Methods of determining whether any particular molecule exhibits those properties are disclosed.

The Applicants need not disclose (and, indeed, have not disclosed) every embodiment of the claimed invention. They need only provide a written description of the invention sufficient to demonstrate possession of the invention. The Examiner correctly recognizes one method of satisfying the written description requirement - by identifying a representative number of species of the claimed invention. However, the Examiner appears to believe that identification of a representative number of species is the only way that the written description requirement may be satisfied. As indicated in the *Eli Lilly* case cited by the Examiner, a genus of compounds can be achieved by "recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus" (43 USPQ 2d at 1406). In the present application, each of the modules for which fragments (derivatives, etc.) are recited is identified by a particular amino acid sequence, and the fragments, derivatives, and other structures are disclosed with reference to the particular sequence. The Applicants respectfully contend that these disclosures identify all of the relevant distinguishing characteristics of the claimed subject matter. These disclosures therefore constitute a sufficient description of the subject matter that the skilled artisan would understand that the Applicants were in possession of the claimed invention at least as of the priority date of the present application.

The Examiner objects to use of the terms "fragment," "derivative,", "substitution," "insertion," "deletion," "exchange," and "addition." In the Examiner's apparent view, these terms broaden the subject matter of the claims beyond the written description provided in the specification, such that at least portions of proteins not explicitly disclosed in the specification might be included. The Examiner concludes that the specification does not adequately describe this subject matter. The Applicants respectfully disagree.

With respect to portions of any protein which might be added to, inserted within, substituted in place of, etc. part of the disclosed polypeptide sequence corresponding to a module

recited in a claim, the identity of that portion is immaterial, so long as it does not interfere with the disclosed function of the module. Thus, the implication from the specification that this portion can correspond to substantially any portion (or even to no protein at all; e.g., corresponding to a random polypeptide sequence) describes the subject matter of the claim in a manner which is co-extensive in scope with the subject matter of the claim. Thus, the subject matter of each claim is disclosed in the specification throughout its scope. Therefore, every claim satisfies the written description requirement. Reconsideration and withdrawal of the Examiner's rejection of claims 1-27, 29, and 34-37 pursuant to the written description requirement of 35 U.S.C. § 112, first paragraph, are respectfully requested.

Rejection of claims 1, 5, 8, 10, 11, 13-16, 26, 34, and 36 pursuant to 35 U.S.C. § 112, second paragraph

Claims 1, 5, 8, 10, 11, 13-16, 26, 34, and 36 have been rejected by the Examiner pursuant to 35 U.S.C. § 112, second paragraph. The Applicants separately discuss the Examiner's rejections of these claims on page 8 of the Office Action in the following paragraphs.

Claims 1, 5, 34, and 36 recite the term "degenerate" in reference to a nucleic acid sequence. In the Examiner's view, the recitation of this term renders the claims indefinite. The Applicants disagree. The term "degenerate" as applied to nucleic acids which encode a polypeptide is well-known in the art and need not be defined in the specification. This term describes the fact that multiple tri-nucleotide codons can encode the same amino acid residue. Therefore, the Applicants contend that use of the term "degenerate" in the context of nucleic acids is not indefinite in view of what is known in the art.

Claims 10 and 11 recite "a cell of the specific immune system," and claim 13 recites "a cell of the unspecific immune system." In the Examiner's view, the meaning of these terms is unclear. The Applicants contend that the skilled artisan would understand the term "a cell of the specific immune system" to refer to an immune cell which expresses a protein on its surface, which protein binds specifically with an antigen. The Applicants further contend that the skilled artisan would understand the term "a cell of the unspecific immune system" to refer to

an immune cell (e.g., a mast cell or hematopoietic stem cell) which does not express an antigen-binding protein on its surface.

The Examiner objects to use of the term "a degenerate cell of the immune system" to describe the tumor cell referred to in claim 14. The Applicants contend that the skilled artisan understands that cells of the immune system are not normally tumor cells, and that tumor cells which exhibit numerous characteristics of immune cells are malfunctioning (i.e., degenerate) immune cells.

The Examiner objects to use of the symbol "/" and the designation "S1' " in claim 8. The Applicants respond that "/" simply refers to the processing site. As explained earlier in this Amendment, "S' " is simply an art-accepted designation for the amino acid residue on the other side of the processing site, as evidenced in the enclosed excerpt from Fersht, (1985, Enzyme Structure and Mechanism, 2d ed., W.H. Freeman and Co., New York, at pp. 29-30). In order to remove any question regarding the meaning of "S1'," the Applicants have amended the claim to explicitly recite that S1' is any amino acid residue. The Applicants respectfully contend that claim 8, as amended, is neither ambiguous or indefinite.

The Examiner objects to the terms "T7-Tag," "Flag-Tag," and "GFP" in claim 15. The first two terms have been replaced by their respective trademark designations, and the common abbreviation 'GFP' has been replaced by "green fluorescent protein."

The Examiner objects to the designation "sp." in claim 26. This common abbreviation has been replaced by "species."

The Examiner objects to allegedly insufficient antecedent bases in claims 15 and 16. The dependency of both claims has been modified to alleviate the Examiner's antecedent basis objection.

The Applicants respectfully contend that each of claims 1, 5, 8, 10, 11, 13-16, 26, 34, and 36 complies with 35 U.S.C. § 112, second paragraph, and that the Examiner should reconsider and withdraw the rejection of each of these claims on this basis.

Rejection of claims 1-27, 29, and 34-37 pursuant to 35 U.S.C. § 103(a)

The Examiner has rejected claims 1-6, 8-14, 16-27, 29, and 34-37 pursuant to 35 U.S.C. § 103(a) in view of the combination of European Patent EP 0751221A1 and Lappi, et al. Claims 7 and 15 stand rejected pursuant to 35 U.S.C. § 103(a) in view of this combination, and further in view of Grisshammer.

The publication date (Veröffenlichungstag) of EP 0751221A1 is January 2, 1997. The effective filing date of the present application is also January 2, 1997 (35 U.S.C. § 365(b); M.P.E.P. §201.13(b)). The Applicants therefore respectfully contend that EP 0751221A1 is not prior art with respect to the present application. The Examiner has not alleged that the Lappi reference, the Grisshammer reference, or the combination of these two references (i.e., not in combination with EP 0751221A1) renders any claim obvious pursuant to 35 U.S.C. § 103(a). The Applicants respectfully request reconsideration and withdrawal of the rejection of claims 1-6, 8-14, 16-27, 29, and 34-37 pursuant to 35 U.S.C. § 103(a).

Summary

The Applicants respectfully submit that each rejection of the Examiner has been overcome or is now inapplicable, and that each of the claims 1-27, 29, and 32-37 is in condition for allowance. Reconsideration and allowance of each of these claims are respectfully requested at the earliest possible date.

Respectfully submitted,
Jürgen Eck et al.

22 November 2000
(Date)

By: _____

GARY D. COLBY, Ph.D., J.D.
Registration No. 40,961
AKIN, GUMP, STRAUSS, HAUER, & FELD, L.L.P.
One Commerce Square – 22nd Floor
2005 Market Street
Philadelphia, PA 19103-7086
Telephone: 215-965-1200
Direct Dial: 215-965-1285
Facsimile: 215-965-1210
E-Mail: GColby@AkinGump.com

Enclosure: Petition for a 3-Month Extension of Time
Pending Claims, as Amended to Date
Fersht, (1985, Enzyme Structure and Mechanism, 2d ed., Freeman, New York)